



spinal muscular atrophy with progressive myoclonic epilepsy

Spinal muscular atrophy with progressive myoclonic epilepsy (SMA-PME) is a neurological condition that causes muscle weakness and wasting (atrophy) and a combination of seizures and uncontrollable muscle jerks (myoclonic epilepsy).

In individuals with SMA-PME, spinal muscular atrophy results from a loss of specialized nerve cells, called motor neurons, in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem). After a few years of normal development, affected children begin experiencing muscle weakness and atrophy in the lower limbs, causing difficulty walking and frequent falls. The muscles in the upper limbs are later affected, and soon the muscle weakness and atrophy spreads throughout the body. Once weakness reaches the muscles used for breathing and swallowing, it leads to life-threatening breathing problems and increased susceptibility to pneumonia.

A few years after the muscle weakness begins, affected individuals start to experience recurrent seizures (epilepsy). Most people with SMA-PME have a variety of seizure types. In addition to myoclonic epilepsy, they may have generalized tonic-clonic seizures (also known as grand mal seizures), which cause muscle rigidity, convulsions, and loss of consciousness. Affected individuals can also have absence seizures, which cause loss of consciousness for a short period that may or may not be accompanied by muscle jerks. In SMA-PME, seizures often increase in frequency over time and are usually not well-controlled with medication. Individuals with SMA-PME may also have episodes of rhythmic shaking (tremors), usually in the hands; these tremors are not thought to be related to epilepsy.

Some people with SMA-PME develop hearing loss caused by nerve damage in the inner ear (sensorineural hearing loss).

Individuals with SMA-PME have a shortened lifespan; they generally live into late childhood or early adulthood. The cause of death is often respiratory failure or pneumonia.

Frequency

SMA-PME is a rare disorder; approximately a dozen affected families have been described in the scientific literature.

Genetic Changes

SMA-PME is caused by mutations in the *ASAH1* gene. This gene provides instructions for making an enzyme called acid ceramidase. This enzyme is found in lysosomes,

which are cell compartments that digest and recycle materials. Within lysosomes, acid ceramidase breaks down fats called ceramides into a fat called sphingosine and a fatty acid. These two breakdown products are recycled to create new ceramides for the body to use. Ceramides have several roles within cells. For example, they are a component of a fatty substance called myelin that insulates and protects nerve cells.

ASAH1 gene mutations that cause SMA-PME result in a reduction of acid ceramidase activity to a level less than one-third of normal. Inefficient breakdown of ceramides and impaired production of its breakdown products likely play a role in the nerve cell damage that leads to the features of SMA-PME, but the exact mechanism is unknown.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- hereditary myoclonus with progressive distal muscular atrophy
- Jankovic-Rivera syndrome
- SMA-PME
- SMAPME

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Jankovic Rivera syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1834569/>

Other Diagnosis and Management Resources

- Muscular Dystrophy Association: Spinal Muscular Atrophy Types
<https://www.mda.org/disease/spinal-muscular-atrophy/types>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>

- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Epilepsy
<https://medlineplus.gov/epilepsy.html>
- Health Topic: Spinal Muscular Atrophy
<https://medlineplus.gov/spinalmuscularatrophy.html>

Genetic and Rare Diseases Information Center

- Jankovic Rivera syndrome
<https://rarediseases.info.nih.gov/diseases/3044/jankovic-rivera-syndrome>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page>
- National Institute of Neurological Disorders and Stroke: Motor Neuron Diseases Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Motor-neuron-diseases-Information-Page>

Educational Resources

- Boston Children's Hospital: Seizures
<http://www.childrenshospital.org/conditions-and-treatments/conditions/s/seizures>
- Boys Town National Research Hospital: Types of Hearing Loss
<https://www.boystownhospital.org/knowledgeCenter/articles/hearing/Pages/TypesofHearing.aspx>
- Cleveland Clinic: Myoclonus
<http://my.clevelandclinic.org/health/articles/myoclonus>
- Disease InfoSearch: Jankovic Rivera syndrome
<http://www.diseaseinfosearch.org/Jankovic+Rivera+syndrome/3897>
- Johns Hopkins Medicine: Myoclonic Seizures
http://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/epilepsy/seizures/types/myoclinic-seizures.html

- Kennedy Krieger Institute: Epilepsy (Seizure Disorder)
<https://www.kennedykrieger.org/patient-care/diagnoses-disorders/epilepsy-seizure-disorder>
- MalaCards: spinal muscular atrophy with progressive myoclonic epilepsy
http://www.malacards.org/card/spinal_muscular_atrophy_with_progressive_myoclonic_epilepsy
- Merck Manual for Patients and Caregivers: Seizure Disorders
<http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/seizure-disorders/seizure-disorders>
- Orphanet: Spinal muscular atrophy-progressive myoclonic epilepsy syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2590
- Washington University, St. Louis: Neuromuscular Disease Center
<http://neuromuscular.wustl.edu/synmot.html#asah1>

Patient Support and Advocacy Resources

- Families of SMA
<http://www.curesma.org/>
- FightSMA
<http://fightsma.org/>
- Muscular Dystrophy UK: Spinal Muscular Atrophy
<http://www.musculardystrophyuk.org/about-muscle-wasting-conditions/spinal-muscular-atrophy-sma/>
- National Organization for Rare Disorders (NORD): Progressive Myoclonus Epilepsy
<https://rarediseases.org/rare-diseases/progressive-myoclonus-epilepsy/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28hereditary+myoclonus%5BTIAB%5D%29+AND+%28progressive+distal+muscular+atrophy%5BTIAB%5D%29+OR+%28sma-pme%5BTIAB%5D%29+OR+%28spinal+muscular+atrophy%5BTIAB%5D%29+AND+%28progressive+myoclonic+epilepsy%5BTIAB%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D>

OMIM

- SPINAL MUSCULAR ATROPHY WITH PROGRESSIVE MYOCLONIC EPILEPSY
<http://omim.org/entry/159950>

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